

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (Previously Presented) A humanized immunoglobulin having binding specificity for B7-2, wherein said immunoglobulin has a binding affinity of at least about $10^7 M^{-1}$, and wherein said immunoglobulin comprises an antigen binding region of non-human origin and at least a portion of an immunoglobulin of human origin, further wherein the antigen binding region of non-human origin comprises at least one framework region containing a substitution of at least one amino acid to a corresponding amino acid in the III2R heavy chain framework region or the H2F light chain framework region.

2. (Previously Presented) The humanized immunoglobulin of Claim 1, wherein the portion of immunoglobulin of human origin is a human constant region.

3. (Original) The humanized immunoglobulin of Claim 2, wherein the human constant region comprises an IgG constant region.

4. (Original) The humanized immunoglobulin of Claim 3, wherein the human constant region contains a mutation capable of reducing the effector function of the immunoglobulin.

5. (Previously Presented) The humanized immunoglobulin of Claim 4, wherein the human constant region comprises an IgG2 constant region and a Valine amino acid at position 234 of the IgG2 constant region is substituted with Alanine and/or a Glycine amino acid at position 237 of the IgG2 constant region is substituted with Alanine.

6. (Original) The humanized immunoglobulin of Claim 3, wherein the IgG constant region is selected from the group consisting of an IgG4 constant region and an IgG2 constant region.

7. (Original) The humanized immunoglobulin of Claim 1, wherein the antigen binding region is of rodent origin.

8. (Previously Presented) The humanized immunoglobulin of Claim 1, wherein the antigen binding region comprises a complementarity determining region of rodent origin, and the portion of an immunoglobulin of human origin is at least a portion of a human framework region.

9. (Previously Presented) The humanized immunoglobulin of Claim 8, wherein the complementarity determining region is derived from the 3D1 monoclonal antibody.

10. (Previously Presented) The humanized immunoglobulin of Claim 1, further comprising a constant region of human origin, wherein the heavy chain comprises a variable region of SEQ ID NO:6 and the light chain comprises a variable region of SEQ ID NO:8.

11. (Previously Presented) The humanized immunoglobulin of Claim 1, wherein said immunoglobulin can compete with the murine 3D1 antibody for binding to B7-2.

12. (Previously Presented) The humanized immunoglobulin of Claim 11, wherein the light and heavy chains each have three complementarity determining regions derived from the 3D1 antibody.

Claims 13-14 (Cancelled)

15. (Previously Presented) A humanized immunoglobulin having a binding specificity for B7-2, wherein said immunoglobulin has a binding affinity of at least about

107 M-1, and wherein said humanized immunoglobulin is derived from the cell line deposited with the ATCC®, Accession No. CRL-12524.

Claims 16-20 (Cancelled)

21. (Previously Presented) A humanized immunoglobulin light chain having binding specificity for B7-2, wherein said immunoglobulin has a binding affinity of at least about 10^7 M^{-1} , and wherein said immunoglobulin comprises CDR1, CDR2 and CDR3 of the light chain of the murine 3D1 antibody, and further wherein the immunoglobulin comprises at least one framework region containing a substitution of at least one amino acid to a corresponding amino acid in the framework region of the light chain of the human H2F antibody.

Claim 22 (Cancelled)

23. (Previously Presented) The humanized immunoglobulin light chain of Claim 21, wherein the light chain comprises a variable region of SEQ ID NO: 8.

24. (Currently Amended) An isolated nucleic acid molecule encoding an immunoglobulin light chain having a binding specificity for B7-2 comprising a nucleotide sequence selected from the group consisting of:

- a) SEQ ID NO:7;
- b) a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:8,
- c) the nucleic acid sequence of a nucleic acid molecule which hybridizes to the complement of the nucleic acid molecule comprising a nucleotide sequence according to a) or b) under stringent hybridization conditions, and

d) a nucleotide sequence which is a complement of the nucleotide sequence according to a) or b).

25. (Currently Amended) A humanized immunoglobulin light chain having binding specificity for B7-2, wherein said immunoglobulin has a binding affinity of at least about 10^7 M^{-1} , and wherein said immunoglobulin comprises CDR1, CDR2 and CDR3 of the heavy chain of the [~~murine~~] murine 3D1 antibody, and further wherein the immunoglobulin comprises at least one framework region containing a substitution of at least one amino acid to a corresponding amino acid in the framework region of the heavy chain of the human H2F antibody.

Claim 26 (Cancelled)

27. (Previously Presented) The humanized immunoglobulin heavy chain of Claim 21, wherein the heavy chain comprises a variable region of SEQ ID NO:6.

28. (Currently Amended) An isolated nucleic acid molecule encoding an immunoglobulin heavy chain having binding specificity of B7-2 comprising a nucleotide sequence selected from the group consisting of:

- a) SEQ ID NO: 5,
- b) a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 6,
- c) the nucleotide sequence of a nucleic acid molecule which hybridizes to the complement of the nucleic acid molecule comprising a nucleotide sequence according to a) or b) under stringent hybridization conditions, and
- d) a nucleotide sequence which is the complement of the nucleotide sequence according to a) or b).

Claim 29 (Cancelled)

30. (Currently Amended) An expression vector comprising a [~~fused gene~~]
nucleic acid encoding a humanized immunoglobulin light chain, said gene comprising a
nucleotide sequence encoding a CDR derived from a nonhuman antibody having
binding specificity for B7-2, wherein said immunogloblin has a binding affinity of at least
about 10^7 M⁻¹, further wherein the immunoglobulin comprises at least one framework
region containing a substitution of at least one amino acid to a corresponding amino
acid in the framework region of the light chain of the human H2F antibody.

31. (Previously Presented) The expression vector of Claim 30, wherein the
nonhuman antibody is the murine 3D1 antibody and a substitution of at least one amino
acid to a corresponding amino acid in the framework region of the heavy chain of the
human III2R antibody.

32. (Original) A host cell comprising the expression vector of Claim 30.

33. (Currently Amended) An expression vector comprising a [~~fused gene~~]
nucleic acid encoding a humanized immunoglobulin heavy chain, said gene comprising
a nucleotide sequence encoding a CDR derived from a nonhuman antibody having
binding specificity for B7-2, wherein said immunogloblin has a binding affinity of at least
about 10^7 M⁻¹, further wherein the immunoglobulin comprises at least one framework
region containing a substitution of at least one amino acid to a corresponding amino
acid in the framework region of the heavy chain of the human III2R antibody.

34. (Previously Presented) The expression vector of Claim 33, wherein the
nonhuman antibody is the murine 3D1 antibody.

35. (Original) A host cell comprising the expression vector of Claim 33.

36. (Previously Presented) A host cell comprising at least one nucleic acid molecule encoding the humanized immunoglobulin of Claim 1.

Claim 37 (Cancelled)

38. (Previously Presented) A method of preparing a humanized immunoglobulin comprising maintaining a host cell of Claim 36 under conditions appropriate for expression of a humanized immunoglobulin, wherein humanized immunoglobulin chains are expressed and a humanized immunoglobulin is produced.

39. (Original) The method of Claim 38, further comprising the steps of isolating the humanized immunoglobulin.

40. (Currently Amended) A [~~fused gene~~] nucleic acid encoding a humanized immunoglobulin light chain having a binding specificity for B7-2, wherein said immunoglobulin has a binding affinity of at least about 10^7 M^{-1} , comprising:

a) a first nucleic acid molecule encoding an antigen binding region derived from the murine 3D1 monoclonal antibody, further wherein the immunoglobulin comprises at least one framework region containing a substitution of at least one amino acid to a corresponding amino acid in the framework region of the light chain of the human H2F antibody; and

b) a second nucleic acid sequence encoding at least a portion of a constant region of an immunoglobulin of human origin.

41. (Withdrawn) A method of inhibiting the interaction of a first cell bearing a B7 2 receptor with a second cell bearing B7-2, comprising contacting said first cell with an effective amount of a humanized immunoglobulin of Claim 1.

42. (Withdrawn) A method of modulating an immune response of a patient having a transplanted organ, tissue, cell or the like comprising administering an effective amount of the humanized immunoglobulin of Claim 1 in a carrier.

43. (Withdrawn) A method for treating a patient having a transplanted organ, tissue or cell, comprising administering a therapeutically effective amount of the humanized antibody of Claim 1.

44. (Withdrawn) The method of Claim 43, wherein the carrier is pharmaceutical carrier.

45. (Withdrawn) A method of treating an autoimmune disease associated with modulation of the B72 molecule, comprising administering to a patient an effective amount of a humanized immunoglobulin of Claim 1 in a carrier, wherein treatment of the autoimmune disease occurs.

46. (Previously Presented) A pharmaceutical composition comprising the antibody of Claim 1 and a pharmaceutically acceptable carrier.

47. (Withdrawn) A method of treating a patient with a disease selected from the group consisting of: autoimmune diseases, infectious diseases, inflammatory disorders, systemic lupus erythematosus, diabetes mellitus, insulinitis, arthritis, inflammatory bowel disease, inflammatory dermatitis, and multiple sclerosis, comprising administering a therapeutically effective amount of a humanized immunoglobulin specific to B7-2 to the patient.

48. (Withdrawn) A method of treating a disease that is modulated by B7-2 comprising administering a therapeutically effective amount of the humanized antibody of Claim 1.

Claims 49 and 50 (Cancelled)

51. (Withdrawn) A method for determining the presence or absence of B7-2 in a sample comprising the steps of:

- a) contacting said sample with a humanized antibody specific to B7-2 sufficiently to allow formation of a complex between B7 2 and the anti B7-2 antibody, and
- b) detecting the presence or absence of said complex formation.

52. (Withdrawn) A method for treating a patient with a disease selected from the group consisting of autoimmune diseases, infectious diseases, inflammatory disorders, systemic lupus erythematosus, diabetes mellitus, insulinitis, asthma, arthritis, inflammatory bowel disease, inflammatory dermatitis, and multiple sclerosis, comprising administering a therapeutically effective amounts of a humanized immunoglobulin specific to B7-1 and a therapeutically effective amount of a humanized immunoglobulin specific to B7-2.

53. (Withdrawn) A method of modulating an immune response of a patient having a transplanted organ, tissue, cell or the like comprising administering an effective amount of the humanized immunoglobulin specific to B7-1 and an effective amount of a humanized immunoglobulin specific to B7-2 in a carrier.

54. (Withdrawn) A method for transplanting cells to a patient in need thereof, comprising:

- a) obtaining cells from a donor,
- b) contacting the cells with an immunoglobulin specific to B7-1, an

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immunoglobulin specific to B7-2 and recipient cells from the patient for a period of time sufficient for tolerance induction, thereby obtaining a mixture, and

c) introducing the mixture to the patient.

55. (Withdrawn) The method of Claim 54, wherein the cells from the donor are derived from bone marrow or blood.

56. (Withdrawn) The method of Claim 55, wherein the recipient cell is a lymphocyte.

57. (Withdrawn) The method of Claim 56, wherein the period of time is between about 12 hours and about 48 hours.

58. (Withdrawn) The method of Claim 57, wherein the period of time is about 36 hours.

59. (Withdrawn) The method of Claim 54, wherein the patient has a disease that is selected from the group consisting of a proliferative disease, anemia and myeloid dysplasia syndrome.

60. (Withdrawn) The method of Claim 59, wherein the proliferative disease is selected from the group consisting of leukemia, lymphoma and cancer.

61. (Withdrawn) The method of Claim 59, wherein the anemia is selected from the group consisting of: sickle cell anemia, thalassemia and aplastic anemia.

62. (Withdrawn) A method for transplanting cells to a patient in need thereof, comprising:

- a) obtaining cells from a donor,
- b) contacting the cells with an immunoglobulin specific to B7-1, an

immunoglobulin specific to B7-2, and tissue, organ or cells that express 5 MHC Class I antigen, B7-1 and B7-2 molecules, for a period of time sufficient for tolerance induction, thereby obtaining a mixture, and

c) introducing the mixture to the patient.

63. (Withdrawn) The method of Claim 62, wherein the cells derived from the donor are derived from bone marrow, stem cells or immature blood cells.

64. (Currently Amended) An expression vector comprising a [~~fused-gene~~] nucleic acid encoding a humanized immunoglobulin light chain, said gene comprising the nucleotide sequence of Claim 24.

65. (Previously Presented) A host cell comprising the expression vector of claim 64.

66. (Currently Amended) An expression vector comprising a [~~fused-gene~~] nucleic acid encoding a humanized immunoglobulin heavy chain, said gene comprising the nucleotide sequence of Claim 28.

67. (Previously Presented) A host cell comprising the expression vector of claim 66.

68. (Previously Presented) The humanized immunoglobulin of Claim 10, wherein the human constant region comprises an IgG constant region.

69. (Previously Presented) The humanized immunoglobulin of Claim 68, wherein the human constant region contains a mutation capable of reducing the effector function of the immunoglobulin.

70. (Previously Presented) A humanized immunoglobulin of Claim 69, wherein the human constant region comprises an IgG2 constant region and a Valine amino acid

at position 234 of the IgG2 constant regions is substituted with Alanine and/or a Glycine amino acid at position 237 of the IgG constant region is substituted with Alanine.

71. (Previously Presented) The humanized immunoglobulin of Claim 68, wherein the IgG constant region is selected from the group consisting of an IgG4 constant region and an IgG2 constant region.

72. (Previously Presented) A host cell comprising at least one nucleic acid molecule encoding the humanized immunoglobulin of Claim 10.

73. (Currently Amended) A method of preparing a humanized immunoglobulin comprising maintaining a host cell of Claim 72 under conditions appropriate for expression of a humanized immunoglobulin, wherein said humanized immunoglobulin chains are expressed and a humanized immunoglobulin is produced.

74. (Previously Presented) The method of Claim 73, further comprising the steps of isolating the humanized immunoglobulin.

75. (Currently Amended) A ~~[fused gene]~~ nucleic acid encoding a humanized immunoglobulin heavy chain having a binding specificity for B7-2, wherein said immunoglobulin has a binding affinity of at least about 10^7 M^{-1} , comprising:

a) a first nucleic acid molecule encoding an antigen binding region derived from the murine 3D1 monoclonal antibody, further wherein the immunoglobulin comprises at least one framework region containing a substitution of at least one amino acid to a corresponding amino acid in the framework region of the heavy chain of the human III2R antibody; and

b) a second nucleic acid sequence encoding at least a portion of a constant region of an immunoglobulin of human origin.

76. (Previously Presented) The humanized immunoglobulin of either of claims 1 or 10 which binds to human B7-2 with an affinity of about $1 \times 10^9 \text{ M}^{-1}$.

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